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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,937	02/16/2006	Naoki Taoka	05432/100L890-US1	1883

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EXAMINER	
KATAKAM, SUDHAKAR	
ART UNIT	PAPER NUMBER
1621	
MAIL DATE	DELIVERY MODE
05/12/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,937	TAOKA ET AL.	
	Examiner	Art Unit	
	Sudhakar Katakam	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 13-111* is/are pending in the application.

4a) Of the above claim(s) *3,6,7,13,15,16,36-50,57-62,69-98 and 108-110* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,8-10,14,17-35,51-56,63-68,99-107 and 111* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the application

1. Receipt of Applicant's remarks and arguments filed on 27th Feb 2009 is acknowledged. In view of applicants' arguments the previous 112 1st rejection has been withdrawn. However, upon further consideration, a new ground(s) of 112 1st rejection is made in view of different interpretation of the previously applied reasoning for the rejection, and provide an explanation of the rejection.

2. However, applicants' arguments for the previous 103(a) rejections are found not persuasive and are maintained for the reasons as set forth in the previous office action.

Claim Objections

3. Claim 52 is objected to because of the following informalities: the name of the enzyme is missing in between "wherein" and "is selected from" in the line 1. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-2, 4-5, 8-10,14, 17-35, 51-56, 63-68, 99-107 and 111 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ 2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (see *Vas-Cath* at page 1116).

In the instant case, the claims are directed to a method for the preparation of S- or R-enantiomer of a diol having the formula (II). As practicing the claimed invention requires selective enzymatic acylation as recited in the claim 1, and the hydrolase enzyme is selected from Pseudomonas sp. lipoprotein lipase, and mutants and variants thereof, a means to obtain the product by enzymatic acylation is a critical element of the claims and must be described according to the requirement of 35 USC § 112, first paragraph.

The claimed enzymes are extremely broad. Are all hydrolase enzymes work for the applicant's claimed acylation reaction process? Applicants provide no written description for the reaction process except Novozyme 435 in the specification.

Applicants also failed to describe the mutants and variants and show no data with mutants and variants for the claimed enzymatic acylation reaction process.

The guidelines for Written Description state "The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art" (Federal Register/Vol.66,No.4/Friday, January 5, 2001/Notices, column 1, page 1105). The guidelines also state, "[t]he claim as a whole, including all limitations found in the preamble, the transitional phrase, and the body of the claim, must be sufficiently supported to satisfy the written description requirement" (at page 1105, center column, third full paragraph). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations. *Lockwood v. American Airlines Inc.* (CA FC) 41 USPQ2d 1961 (at 1966).

The Guidelines for Written Description further state: "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus" (Federal Register, Vol.66,No.4, Column 3, page 1106). "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction of practice…., reduction to drawings…., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus" (MPEP 2163(3)(a)(ii)).

In contrast, the instant application fails to disclose in specific terms even a single enzymatic acylation using an acylating agent. Also, in the instant case, the teachings of the specification with regard to Pseudomonas sp. lipoprotein, and mutants and variants thereof, are the source for the hydrolase enzyme. Beyond this, the application provides no guidance to how these mutants and variants are source for the hydrolase enzyme. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only a limited number of species within the genus.

The possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. *Ex parte Kubin*, 83 USPQ2d 1410, 1417 (Bd. Pat. App. & Int. 2007) citing *University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895,

Thus, claiming a method using any enzyme in enzymatic acylation using an acylating agent that achieves a result without defining what means will do is not in compliance with the written description requirement. Rather, it is attempted to preempt the future before it has arrived. With regard to the mutants and variants, failure of the application to disclose which mutants and variants are the source for hydrolase enzyme, the skilled artisan would not have viewed the disclosure as demonstrating possession of the broad scope of any enzyme, and mutants and variants of Pseudomonas sp. lipoprotein thereof, having the source of hydrolase enzyme as recited in the claim. Therefore, the claims are properly

rejected under 35 USC 112 first paragraph, as lacking adequate written description.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

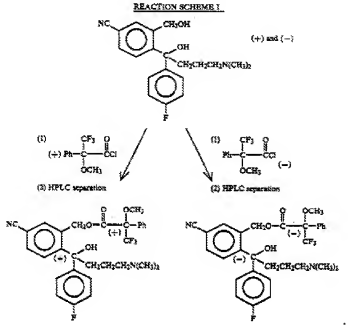
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 1-2, 4-5, 8-10,14, 17-35, 51-56, 63-68, 99-107 and 111 are again rejected under 35 U.S.C. 103(a) as being unpatentable over **Boegesoe et al** (US 4,943,590) in view of **Sturmer** (US 6,551,806) and **Takano et al** (US 5,219,743).

Boegesoe et al teach the following scheme for the preparation of S- or R-enantiomer of a diol of the following formula:



The differences between the instant claims and **Boegesoe et al** are as follows:

(i) **Boegesoe et al** fails to teach the enzymatic acylation with a hydrolase enzyme for the preparation of S- or R-enantiomer of a diol of formula (II) of claim 1.

(ii) **Boegesoe et al** fails to teach the applicants solvent for the process.

With regard to (i) of above, **Sturmer** teaches enzyme containing polymers are used as catalysts in chemical reactions such as acylation or enantioselective acylation of alcohols [col.10, lines 27-35] with a preferred carboxylic acid ester as acylating agents are vinyl esters [col.12, lines 13-28]. Enzyme, such as hydrolase, preference is given to lipases from Pseudomonas sp. [col. 3, lines 8-65].

With regard to (ii) of above, **Takano et al** teach a method for optical resolution of corey lactone diols with an acylating agent in the presence of enzyme, such as lipase from Pseudomonas sp. [col.2 lines 41-68]. **Takano et al** also teach that any solvent may be used so long as it does not inactivate the enzyme and does not react with the substrate and the ester produced [col.4, lines 34-39].

In summary, **Boegesoe et al** teach the preparation of S- or R-enantiomer of a diol from its racemic mixture using enzymatic acylation with hydrolase. **Sturmer** teaches enzyme, Such as lipases, containing polymers are used as catalysts in chemical reactions such as acylation or enantioselective acylation of alcohols with a preferred carboxylic acid ester as acylating agents are vinyl esters. **Takano et al** teach that any solvent may be used so long as it does not inactivate the enzyme and does not react with the substrate and the ester produced in the process of optical resolution of corey lactone diols with an acylating agent in the presence of enzyme.

The claims would have been obvious because, a person of ordinary skill has a good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product, not of innovation, but of ordinary skill and common sense.

The claim would have been obvious because the design incentives or market forces provided a reason to make an adaptation,

and the invention resulted from application of the prior knowledge in a predictable manner.

All the claimed elements were known in the prior art and one skilled person in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to have yielded predictable results to one of ordinary skill in the art at the time of the invention.

In view of explicit teachings of the cited references, the examiner asserts that it would have been obvious to a person of ordinary skill in the art, at the time of invention was made, to have combined the teaching of references to make the instantly claimed process with a reasonable expectation of success. The selection of acylating agent, enzyme source and the solvent is within the purview of an ordinary artisan.

Modifying such methodology is prima facie obvious because an ordinary artisan would be motivated to use known preparation methods to make the process more efficient or explore economical advantages over the other, since it is within the scope to optimize the conditions through routine experimentation. Merely modifying the process conditions such as using alternative acylating agents or enzymes or solvents, is not a patentable modification absent a showing of criticality.

Response to Arguments

9. Applicant's arguments filed on 27th Feb have been fully considered but they are not persuasive.

The examiner acknowledges applicants' argument that "the present specification provides an extensive and detailed description of how enzymatic acylation is carried out according to the present invention".

The examiner contends, however, that specification showed enzymatic acylation with only one enzyme, which is Novazyme 435. However, claimed enzymes are extremely broad. Applicants failed to provide sequence information for the mutants and variants and also no examples provided for the enzymatic acylation.

The examiner acknowledges applicants' argument that Boegesoe does not teach a process of isolating an S- or R-diol from it racemic mixture, but instead discloses the use of a racemic diol to make an S- or R-ester derivative that can be converted to S- or R-citalopram; and Boegesoe also makes no mention of enzymatic acylation.

The examiner contends, however, that Boegesoe does teach the isolation of S- or R-citalopram from its racemic mixture [see the Reaction Scheme 1]. Applicants claims do not exclude the ester derivative, because claim language says "comprises", which can be interpreted as the process have additional steps in the reaction. Examiner agrees that Boegesoe do not teach the enzymatic acylation. However, the secondary references cure this deficiency.

The examiner acknowledges applicants' argument that presently claimed formula (II) diol has a significantly different and more complicated structure than any starting substrate in Sturmer.

The examiner contends, however, that Sturmer clearly suggested "There is virtually no restriction in relation to the alcohols. Thus, it is possible to use monohydric and polyhydric alcohols such as...." [see col.11, lines 53-65].

The examiner acknowledges applicants' argument that Takano does not disclose separation of enantiomers from a racemic mixture, but instead discloses a mixture of two different diol enantiomers having different molecular formulae.

The examiner contends, however that the purpose of Takano in the office action to show the compatibility of solvents for the enzymatic acylation.

Applicants show how the cited references differ from the instant invention, but the obviousness test under 35 U.S.C. 103 is whether the invention would have been obvious in view of the prior art taken as a whole. **In re Metcalf et al. 157 U.S.P.Q. 423.**

The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it is permissible for the Examiner to rely on disclosures, which

fairly teach embodiments of Applicant's invention. The claims require a multitude of elements and it is reasonable for one of ordinary skill in the art to consider these elements being used together.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sudhakar Katakam whose telephone number is 571-272-9929. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Daniel Sullivan can be reached on 571-272-0779. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sudhakar Katakam/
Examiner, Art Unit 1621

/Peter G O'Sullivan/
Primary Examiner, Art Unit 1621